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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/768,093	02/02/2004	Marcia K. Wolf	034047.033.4	6121

7590 03/20/2007

Office of the Staff Judge Advocate
U.S. Army Medical Research and Materiel Command
ATTN: MCMR-JA (Ms. Elizabeth Arwine)
504 Scott Street
Fort Detrick, MD 21702-5012

EXAMINER	
GRASER, JENNIFER E	
ART UNIT	**PAPER NUMBER**
1645	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/768,093	WOLF ET AL.	
	Examiner	Art Unit	
	Jennifer E. Graser	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *After Final 2/28/07*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. The After Final Amendment submitted 2/28/07 will be entered. The finality of the previous action is withdrawn due to the newly presented rejections.

Claims 16-22 are currently pending.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 16-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wolf et al (different inventive entity) (Submitted. Jan. 1994. UniProt Accession # P53509) in view of Wood (Guide to Molecular Cloning Techniques. Vol. 152. 1987. Section IX. Chapter 49, pages 443-457) and further in view of Wolf et al (1989, Infect.Immun. 57(1): 164-173.

Wolf et al disclose the amino acid sequence of a polypeptide which is 100% identical to Applicants' SEQ ID NO: 9. Wolf et al teach that the amino acid sequence disclosed that the amino acid sequence is a CS6 fimbrial subunit A precursor (CS6 pilin), named 'cssA, isolated from E.coli. However, the amino acid sequence disclosed by Wolf et al contains the N-terminal signal sequence so it is 18 amino acids longer than that of Applicant's SEQ ID NO:9 which does not contain the signal sequence. It was

well known in the prior art at the time the invention was made that the N-terminal, hydrophobic sequences which are mediate the attachment of newly translated polypeptide chains to intracellular membranes in secretory proteins, such as the one which is claimed, is cleaved off during expression. See 'http://crisp.cit.nih.gov/Thesaurus/00006706.htm'. The Wolf et al reference specifically recites that amino acids 1-18 are the 'signal peptide'. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made that to express the protein and achieve the protein minus the signal sequence, which would be identical to SEQ ID NO:9. The recombinant expression methods known in the art were well known at the time the invention was made.

Although the amino acid sequence represented in the computer database is a constructive reduction to practice, Wolf et al do not actually teach a "purified polypeptide" in a method to raise an antigenic response as now claimed.

Wood discloses techniques for gene cloning based on long oligonucleotide probes. It is disclosed that the most commonly used technique for gene cloning has been to utilize oligonucleotide probes based on protein sequence data (page 443, first paragraph). This technique requires at least a portion of the amino acid sequence to be determined so that one can use it to infer the corresponding DNA (page 443, first paragraph). Based on the amino acid sequence information, either short or long oligonucleotide probes can by synthesized chemically. It is disclosed that the utility of the long, single sequence probes has been used repeatedly for the screening of high-complexity libraries starting with any stretch of protein sequence data (page 444, first

full paragraph). Several methods were notoriously well known in the prior art for obtaining the DNA which encodes a known protein sequence and it would have been obvious to use any of them in order to obtain the DNA for the protein disclosed by Wolf et al in order to recombinantly produce the protein. For example, the DNA could be obtained by PCR amplification of the sequence corresponding to the cssA protein disclosed by Wolf. Alternatively, one could clone the protein by generating probes based on the protein sequences as taught by Wood described above, or, even simply deduce a degenerate DNA sequence from the recited amino acid sequence. The insertion of this sequence into a vector for recombinant production in a host bacterial cell was notoriously well known in the prior art at the time the invention was made and one of ordinary skill in the art would have been motivated to do so to investigate this protein for research activities or to use it to raise an immunogenic/antigenic response or as a diagnostic reagent.

Wolf et al. (1989) disclose compositions that comprise CS6 protein from *E.coli* E8775, the same strain from which the protein of SEQ ID NO: 9 was isolated. One of the disclosed compositions that comprised CS6 proteins was an agarose gel containing the CS6 16 kDa band (Figure 3, a type of acceptable carrier). An additional composition that comprised the W8775 CS6 protein was a saline extract of E8775 (see page 167, col. 1, paragraph 1). The protein was used to generate antisera, e.g., an antigenic response. Additionally, it was shown that the whole cell bacterium raised antibodies against the CS6 protein.

It would have been obvious to one of ordinary skill in the art at the time the invention was made that the polypeptide disclosed by Wolf et al (1994) could be recombinantly produced and the host cell expressing the protein or the isolated protein itself could be used to raise an antigenic immune response, particularly because Wolf et al (1989) teach that the same or similar protein could be used to generate antisera. It is noted that the instant specification provides no examples of the in vivo or in vitro use of the methods instantly claimed. Accordingly, the combined references teach at least as much as was shown in the specification, if not more since they actually demonstrate the raising of an immunogenic response. It would have been obvious to one of ordinary skill in the art at the time the invention was made that this recombinant host cell taught by the combination of references could be live, attenuated or killed since the claimed methods only teach 'inducing [*a non-specific*] antigenic response and the specification fails to demonstrate any working examples. It is noted that an enablement rejection was not made because a protein of the size set forth in SEQ ID NO:9 which is a fimbrial protein would be expected to generate some sort of antigenic response as claimed. The administration methods recited in claims 20-22 were all routinely used at the time the invention was made and would have been obvious design choices. They would each be expected to work equally as well at generating a [*non-specific*] antigenic response.

Claim Rejections - 35 USC § 102/103

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 16-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Wolf et al (1989, Infect.Immun. 57(1): 164-173) or, in the alternative, under 35 U.S.C. 103(a) as obvious over by Wolf et al (1989, Infect.Immun. 57(1): 164-173).

Wolf et al. disclose compositions that comprise CS6 protein from *E.coli* E8775, the same strain from which the protein of SEQ ID NO: 9 was isolated. One of the disclosed compositions that comprised CS6 proteins was an agarose gel containing the CS6 16 kDa band (Figure 3, a type of acceptable carrier). An additional composition that comprised the W8775 CS6 protein was a saline extract of E8775 (see page 167, col. 1, paragraph 1). Column 2 on page 164 teaches that the Cs6 gene was recombinantly expressed in a host cell. The protein was used to generate antisera. Additionally, it was shown that the whole cell bacterium raised antibodies against the CS6 protein. Wolf et al do not disclose the amino acid sequence of E8775 16kDa protein CS6, but the amino acid sequence of a protein is an inherent structural characteristic. Inherently the reference anticipates the now claimed invention. Atlas Powder Co. V IRECA, 51 USPQZd 1943, (FED Cir. 1999) states Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior arts functioning, does not render the old composition patentably new to the discoverer. The Court further held that this

same reasoning holds true when it is not a property but an ingredient that is inherently contained in the prior art.

The disclosed protein of the prior art reference appears to be identical to Applicants' protein given the identity of the source, its molecular weight and functional characteristics. Since the Patent Office does not have the facilities for examining and comparing Applicant's protein with the protein of the prior art, the burden of proof is upon applicants to show an unobvious distinction between the material structural and functional characteristics of the claimed protein and the protein of the prior art. See In re Best, 195 USPQ 430, 433 (CCPA 19&&). It would have been obvious to one of ordinary skill in the art at the time the invention was made that the polypeptide disclosed by Wolf et al (1994) could be recombinantly produced and the host cell expressing the protein or the isolated protein itself could be used to raise an antigenic immune response. It is noted that the instant specification provides no examples of the in vivo or in vitro use of the methods instantly claimed. Accordingly, the reference teaches at least as much as was shown in the specification, if not more since they actually demonstrate the raising of an immunogenic response. It would have been obvious to one of ordinary skill in the art at the time the invention was made that this recombinant host cell taught by the reference could be live, attenuated or killed since the claimed methods only teach 'inducing [*a non-specific*] antigenic response and the specification fails to demonstrate any working examples. It is noted that an enablement rejection was not made because a protein of the size set forth in SEQ ID NO:9 which is a fimbrial protein would be expected to generate some sort of antigenic response as claimed. The administration

methods recited in claims 20-22 were all routinely used at the time the invention was made and would have been obvious design choices. They would each be expected to work equally as well at generating a [*non-specific*] antigenic response.

Response to Applicants' Arguments:

Applicants recite that is unknown whether the protein at the 16kDa band in Figure 3 of Wolf et al is CssA, CssB or both, so it can't teach a purifed CssA. They also argue that Wolf et al do not teach or suggest that CS6 is a 4 subunit protein, therefore, one skilled in the art would not be motivated to purify CssA from CssB. These arguments have been fully and carefully considered but are not deemed persuasive. First, the protein would not be both CssA and CssB because each subunit is between ~15-16kDa and the single band is 16kDA (not 30-32kDA) so there would be no need to purify the two subunits from one another. Second, Applicants have agreed that the subunit could be either CssA or CssB. It is irrelevant that Wolf et al do not teach that CS6 is a 4 subunit protein. Wolf teach a purified protein which matches the physical and functional characteristics of the CssA protein. They have failed to provide any evidence that the protein is not the same protein, other than a statement in the amendment that it is unlikely to be. It could just as likely be CssA as CssB. the burden of proof is upon applicants to show an unobvious distinction between the material structural and functional characteristics of the claimed protein and the protein of the prior art. See In re Best, 195 USPQ 430, 433 (CCPA 19&&).

Applicants argue that Wolf et al does not teach the polypeptide because a polypeptide similar to SEQ ID NO:9, such as #P533509, would be expected to result in

an eluted band in a gel in a position substantially similar to SEQ ID NO:9. They argue that the protein of the diluted band could be easily mistaken for one or the other without a suitable control and thus, it is unclear that the protein of the eluted band is SEQ ID NO:9 rather than #p53509. They argue that Wolf et al does not disclose the sequence of the eluted band used to generate the antisera. These arguments have been fully and carefully considered but are not deemed persuasive. Applicants have not shown that the protein taught by Wolf et al does not elute in a gel in a similar position to that of SEQ ID NO:9.

Wolf et al do not disclose the amino acid sequence of E8775 16kDa protein CS6, but the amino acid sequence of a protein is an inherent structural characteristic. Inherently the reference anticipates the now claimed invention. Atlas Powder Co. V IRECA, 51 USPQZd 1943, (FED Cir. 1999) states Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior arts functioning, does not render the old composition patentably new to the discoverer. The Court further held that this same reasoning holds true when it is not a property but an ingredient that is inherently contained in the prior art. Wolf et al. disclose compositions that comprise CS6 protein from *E.coli* E8775, the same strain from which the protein of SEQ ID NO: 9 was isolated. One of the disclosed compositions that comprised CS6 proteins was an agarose gel containing the CS6 16 kDa band (Figure 3, a type of acceptable carrier). An additional composition that comprised the W8775 CS6 protein was a saline extract of E8775 (see page 167, col. 1,

paragraph 1). The protein was used to generate antisera. Additionally, it was shown that the whole cell bacterium raised antibodies against the CS6 protein.

6. Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Remsen. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is 571-273-8300 which is able to receive transmissions 24 hours/day, 7 days/week.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (571) 272-0858. The examiner can normally be reached on Monday-Thursday from 7:30 AM-6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached on (571) 272-0787.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0500.

Jennifer Graser
Primary Examiner
Art Unit 1645

3/17/07